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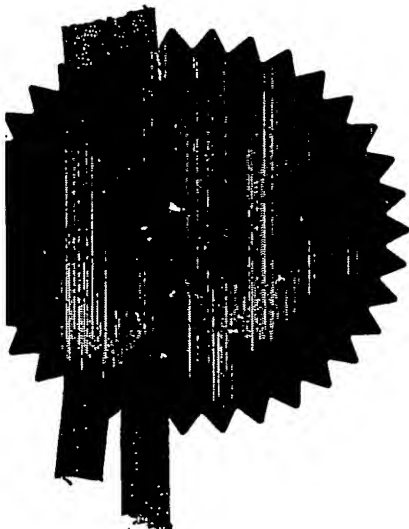
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University of Sheffield  
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SHEFFIELD  
S10 2TN  
GB

Patents ADP number (if you know it)

If the applicant is a corporate body, give the country/state of its incorporation

7396831001

## 4. Title of the invention

SURFACE

## 5. Name of your agent (if you have one)

Harrison Goddard Foote

"Address for service" in the United Kingdom to which all correspondence should be sent (including the postcode)

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Dr Rob Docherty

01904 732120

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## SURFACE

The invention relates to a method to manufacture a non-uniform plasma polymerised surface and products comprising a surface obtainable by said method.

5

Molecular architecture is the formation of three-dimensional structures of polymeric material on surfaces that have controllable levels of crosslinking, frictional wear or solubility characteristics. Chemical architecture refers to the engineering of chemical functionality (the presence of certain reactive moieties, or groups). These surfaces  
10 may have utility in assay products, mass spectrometer probes, microfluidic systems, or in microarray devices, or in micromachines as valves, switches, or pumps.

Currently the use of solid phase assay systems has greatly facilitated the processing and/or analysis of multiple biological samples. This has become a highly automated  
15 methodology. Typically, solid phase assays comprise either the immobilisation of the agent to be assayed on a solid, or at least semi-solid, surface or the immobilisation of agents used to assay a biological agent. The results derived from such assays have greatly assisted clinicians in their diagnosis of various human disorders. They have also enabled environmental authorities to monitor the presence of environmental  
20 pollutants and the presence of various infectious agents that may be present in our environment and/or food. Assays of this type are often laborious and time consuming. It is important that assays are sensitive and reliable.

Genomics analysis involves the analysis of sequence information (DNA, RNA or  
25 protein) typically generated from genome sequencing projects. Typically biomolecules immobilised for this purpose are referred to as microarrays. An array is a two-dimensional sheet to which is applied different biomolecules at different sites on the sheet. This facilitates the screening of the biomolecules in parallel and on a much smaller scale than conventional solid phase assays. Typically biomolecules are  
30 immobilised by chemical coupling or adsorption. Currently arrays of biomolecules are made by depositing aliquots of sample under conditions which allow the

molecules to bind or be bound to the array surface. Alternatively, or in addition, biomolecules maybe synthesised at the array surface and directly or indirectly immobilised. The number of different samples that are applied to a single array can reach thousands. The application of samples to form an array can be facilitated by the use of "array printers", (for example see Gene Expression Micro-Arrays, A New Tool for Genomics, Shalon, D, in Functional Genomics, IBC library series; Southern EM, DNA Chips: Analysing Sequence by Hybridisation to Oligonucleotides on a Large Scale, Trends in Genetics, 12: 110-5, 1996). The analysis of micro-arrays is undertaken by commercially available "array readers" which are used to interpolate the data generated from the array, for example as disclosed in US5, 545, 531. Arrays are typically made individually and used only once before being disposed of. Therefore, it is highly desirable to produce arrays which are manufactured to a high degree of reproducibility and with minimum error.

Similarly the recent genomics projects have generated a substantial amount of protein sequence information. This has greatly facilitated structure/function analysis of proteins to assist in the assigning of function to novel protein sequences. Typically this sort of analysis is referred to as proteomics.

Microarray substrates are typically manufactured from glass, plastics (e.g. polyethylene terephthalate, high density polyethylene, low density polyethylene, polyvinyl chloride, polypropylene or polystyrene); nitrocellulose, nylon.

Typically, solid phase assays are conducted in assay dishes containing multiple wells that are coated with the molecule of interest. These multi-well application dishes are normally manufactured either from glass or plastics that may have variable affinity for the molecule(s) of interest. Plastics used in the manufacture of assay products include polyethylene terephthalate, high density polyethylene, low density polyethylene, polyvinyl chloride, polypropylene or polystyrene.

30

Multi-well dishes can be treated chemically to improve their affinity and/or retention of selected molecules at their surface. It is, of course, highly desirable that the treated surface binds with the target molecule with high affinity and retention but also allows the bound molecule to retain most, if not all, of its biological activity thereby  
5 providing a sensitive and reliable assay.

An example of such a treatment regime for solid phase surfaces is described in GB2016687. The patent describes the treatment of binding surfaces with polysaccharides. Surfaces treated in this way show increased affinity for both  
10 antibodies and antigens. WO8603840 describes solid phase assay surfaces manufactured from specialised resins as an alternative to the use of assay containers manufactured from plastics such as polystyrene. Specifically, WO8603840 discloses the use of the fluorinated resin polytetrafluoroethylene. WO9819161 describes the coating of solid phase assay surfaces with polyethyleneimine. The treated surfaces  
15 show low levels of non-specific adsorption and a high concentration of binding of the target molecule.

Microfluidic systems are scaled-down fluid flow devices, in which the dimensions of the device are such that the surface tension forces dominate that of gravity. As a  
20 result of this, the properties of the internal surfaces of the device have a massive influence on the efficacy of the device. Typically a microfluidic device is constructed from a polymer, such as polycarbonate, or from silicon.

Also, a "lab on a chip" is a scaled down laboratory experiment, or series of  
25 experiments which allows conventional techniques to be applied on a small scale.

In WO01/31339 we disclose the treatment of products by plasma polymerisation.

Plasma polymerisation is a technique which allows an ultra-thin ( eg ca.200nm) cross  
30 linked polymeric film to be deposited on substrates of complex geometry and with controllable chemical functionality. As a consequence, the surface chemistry of

materials can be modified, without affecting the bulk properties of the substrate so treated. Plasmas or ionised gases are commonly excited by means of an electric field. They are highly reactive chemical environments comprising ions, electrons, neutrals (radicals, metastables, ground and excited state species) and electromagnetic radiation. At reduced pressure, a regime may be achieved where the temperature of the electrons differs substantially from that of the ions and neutrals. Such plasmas are referred to as "cold" or "non-equilibrium" plasmas. In such an environment many volatile organic compounds (eg volatile alcohol containing compounds, volatile acid containing compounds, volatile amine containing compounds, or volatile hydrocarbons, neat or with other gases, eg Ar, have been shown to polymerise (H.K. Yasuda, Plasma Polymerisation, Academic Press, London 1985) coating both surfaces in contact with the plasma and those downstream of the discharge. The organic compound is often referred to as the "monomer". The deposit is often referred to as "plasma polymer". The advantages of such a mode of polymerisation potentially include: ultra-thin pin-hole free film deposition; plasma polymers can be deposited onto a wide range of substrates; the process is solvent free and the plasma polymer is free of contamination. Under conditions of low power, plasma polymer films can be prepared which retain a substantial degree of the chemistry of the original monomer. For example, plasma polymerised films of acrylic acid contain the carboxyl group [1]. The low power regime may be achieved either by lowering the continuous wave power, or by pulsing the power on and off.

Co-polymerisation of one or more compounds having functional groups with a hydrocarbon allows a degree of control over surface functional group concentrations in the resultant plasma copolymer (PCP). Suitably, the monomers are ethylenically unsaturated. Thus the functional group compound maybe unsaturated carboxylic acid, alcohol or amine, for example, whilst the hydrocarbon is suitably an alkene. By plasma polymerisation, it is also possible to deposit ethylene oxide-type molecules (eg. tetraethyleneglycol monoallyl ether) to form 'non-fouling' surfaces [2]. It is also possible to deposit perfluoro-

compounds (i.e. perfluorohexane, hexafluoropropylene oxide) to form hydrophobic/superhydrophobic surfaces.

This technique is advantageous because the surfaces have unique chemical and physical characteristics. For example, the surfaces have increased affinity for biological molecules exposed to said surface and allow the assaying of the bound molecule. The surfaces are uniform and enable the reproducible and sensitive assaying of biological molecules bound to the surface. Similarly, the surface wettability, adhesion and frictional/wear characteristics of the substrate can be modified in a controllable and predictable manner.

The technique disclosed in WO01/31339, although effective with respect to providing uniform plasma polymerised surfaces to which biomolecules bind with specificity and affinity, is not sufficiently versatile to provide a surface which has diverse chemical or physical properties.

The method herein disclosed allows the provision of surfaces that are non-uniform and define local surface regions that have different chemical and/or physical properties. We refer to these surfaces as "patterned" in both chemistry and topography. The effect is achieved by drawing off a proportion of the plasma through a micrometre scale orifice or orifices which is translated across the surfaces to be patterned. Alternatively, a plasma may be excited at the tip, or within a microcapillary which can then be used to "write" the molecular architecture and chemistry onto the surface. Chemistry and molecular architecture may be varied vertically (Z-direction) and/or laterally (X-Y plane) by changing the key plasma parameters (power, flow rate, pulse duty cycle or monomer composition), or by altering the portion of the plasma 'drawn off' by physical, electrical or magnetic means during writing. These surfaces allow the immobilisation of different molecules and concentrations of molecules at a micron scale. Similarly, this technique may be used to control the local wettability, adhesion and frictional/wear characteristics on a surface, and have application in microfluidics.



The combination of chemistry and topography permits the fabrication of micrometre scale structures that can act as switches, valves and pumps.

5 We herein disclose a method we refer to as "plasma writing" which provides surfaces that are characterised by chemical and structural micropatterns or gradients extending, typically into three dimensions, wherein the X-Y plane is defined by the surface, and the Z-direction is substantially perpendicular thereto. The invention relates to a method of creating both chemical and molecular architectures onto a  
10 surface, to give rise to two or three-dimensional patterns, without the need to prefabricate masks or stencils, as described in Dai *et al* and without limitation in the number or type of different architectures created on a single surface as part of the same process.

15 According to an aspect of the invention there is provided a method to deposit a non-uniform plasma polymerised surface to a substrate.

Non-uniform refers to surfaces which have a heterogeneous chemical and/or physical structure.

20

According to a further aspect of the invention there is provided a method to prepare at least part of at least one surface of a substrate comprising; depositing on said surface at least one plasma monomer wherein during deposition of said monomer, means are provided which move the monomer source across a surface to be treated to  
25 manufacture a non-uniform polymer surface.

In a preferred method of the invention said means moves a substrate relative to said monomer source.

30 In an alternative method of the invention said means moves said monomer source relative to said substrate.

The substrate and plasma source are affixed to either side of a precision XYZ translation stage. The XYZ stage comprises one fixed and one travelling flange. Therefore, the substrate and plasma source are moved relative to each other.

5

The invention herein disclosed enables the deposition of plasma polymers with different chemistries and molecular architecture in a spatially restricted pattern, optionally at varying concentration, and at a micrometer resolution. This allows the production of products with highly defined chemical and physical surface properties which advantageously; facilitates the binding and/or separation of different biological molecules and different concentrations of biological molecules followed by their detection and analysis; locally modifies the surface characteristics such as wettability, friction and wear, and adhesion; and fabricates structures which through a combination of chemistry and structure act as switches, valves or pumps (upon receipt of an appropriate stimulus).

15

In a preferred method of the invention there is provided a surface comprising two or more polymers formed from at least two monomers, preferably a plurality of polymers formed from a plurality of monomers.

20

In a further preferred method of the invention said surface comprises at least one polymer of at least one monomer wherein the concentration of said polymer is non-uniform across said surface, or part thereof.

25

In a further preferred method of the invention, said surface comprises of two or more polymers of two or more monomers, wherein the concentration of at least one polymer is non-uniform across said surface, or part thereof.

30

In a further preferred method of the invention said monomer is a volatile alcohol.

In an alternative method of the invention said monomer pattern is a volatile acid.

In a still further alternative method said monomer is a volatile amine.

In a further method of the invention said monomer is a volatile hydrocarbon.

5

In a yet further preferred method of the invention said monomer is a volatile fluorocarbon.

10

In a still further preferred method of the invention said monomer is an ethyleneoxide-type molecule.

In a further preferred method of the invention said monomer is a volatile siloxane.

15

In yet still a further preferred method of the invention said monomer is at least one of selected from the group consisting of: allyl alcohol; acrylic acid; octa-1,7-diene; allyl amine; perfluorohexane; tetraethyleneglycol monoallyl ether; or hexamethyl disiloxane (HMDSO).

20

In a further preferred method of the invention said polymer consists of a single monomer.

Preferably the monomer consists essentially of an ethylenically unsaturated organic compound.

25

Preferably the monomer consists of essentially of a single ethylenically unsaturated organic compound.

Preferably the monomer consists of an ethylene oxide type molecule. (e.g. Triglyme)

30

Preferably the compound is an alkene (eg containing up to 20 carbon atoms and more usually up to 12 carbon atoms, eg 8), a carboxylic acid ( especially  $\alpha,\beta$  - unsaturated

carboxylic acid, for example acrylic or methacrylic acid); an alcohol ( especially an  $\alpha,\beta$  - unsaturated alcohol); or an amine ( especially an  $\alpha,\beta$  - unsaturated amine).

5 Preferably the monomer consists of a mixture of two or more ethylenically unsaturated organic compounds.

10 Preferably the compounds are selected from the group consisting of: an alkene (eg containing up to 20 carbon atoms and more usually up to 12 carbon atoms, eg 8), a carboxylic acid ( especially  $\alpha,\beta$  - unsaturated carboxylic acid); an alcohol (especially an  $\alpha,\beta$  - unsaturated alcohol); or an amine ( especially an  $\alpha,\beta$  - unsaturated amine).

15 "Alkene" refers to linear and branched alkenes, of which linear are preferred, containing one or more than one C=C double bond eg an octadiene such as octa-1,7-diene. Dienes form a preferred class of alkenes.

Alternatively said polymer is a co-polymer. Preferably said co-polymer comprises at least one organic monomer with at least one hydrocarbon. Preferably said hydrocarbon is an alkene, eg a diene such as, for example octa 1,7-diene.

20 The method also encompasses the use of other compounds to form plasma, for example and not by way of limitation, ethylamine; heptylamine; methacrylic acid; propanol.

25 In a preferred method of the invention said monomer (s) is/are deposited on said surface in spatially separated dots.

In a further preferred method of the invention said monomer (s) is/are deposited on said surface in tracks or lines.

30 In a yet further preferred method of the invention, said dots and/or lines may be of different polymer chemistry.

In a still further preferred method of the invention, the of the line, track or dot may be non-uniform along its length and in height.

- 5 In a yet further preferred method of the invention, the line or track may be in the form of loops or closed circuits.

- 10 In a yet further preferred method of the invention regions which do not consist of a deposited polymer may be comprised of polymerised ethylene-oxide type monomer providing a non-binding surface.

- 15 In a preferred method of the invention said plasma is sustained under low power conditions, from which are obtainable films containing the original monomer chemistry. Typically, low power conditions refer to a continuous wave power of <10Watts, or the equivalent time-averaged power in the case of pulsed plasmas.

According to a further aspect of the invention there is provided a substrate comprising a surface obtainable by the method according to the invention.

- 20 Preferably said substrate is selected from the group consisting of: glass; plastics (e.g. polyethylene terephthalate, high density polyethylene, low density polyethylene, polyvinyl chloride, polypropylene or polystyrene); nitrocellulose, or nylon, metal or silicon wafer.

- 25 In a preferred embodiment of the invention said substrate is part of an assay product.

In a further preferred embodiment of the invention said assay product is a microarray.

- 30 In an alternative preferred embodiment said assay product is microtitre plate.

In an alternative preferred embodiment said product is a probe component for use in a mass spectrometer.

5 In an alternative preferred embodiment said substrate comprises a microfluidic device, or a part thereof (e.g. valve, switch, guide channel, binding site, pump).

10 It will be apparent that the invention relates to the provision of plasma surfaces that are physically non-uniform and which we refer to as "patterned". The invention relates to the provision of surfaces of more than one single patterned chemistry (indeed, there is no practical limit on the number) that can be 'drawn' with micrometre precision. Such surfaces cannot be obtained by the stencil approach of Dai *et al* [3].

15 Patterns may consist of lines, circles, loops, arrays, or any conceivable geometric shape in any combination on a scale from centimetres down to around 5 microns. This includes 3-dimensional patterns where the material along the z-axis (height) also exhibits chemical and physical differences. As such, nanometer features may be 'grown' on surfaces which comprise different strata of "chemistry" on different local regions of the surface.

20 Alternatively or in combination therewith, by manipulation of the plasma during the process, a pattern may be written that has along its length a variable concentration of polymer or plasma, which is herein referred to as a "gradient surface", typically a microgradient. The invention encompasses surfaces comprising multiple polymers  
25 deposited in a controlled manner.

According to a yet further aspect of the invention there is provided an assay product according to the invention for use with an array printer.

30 According to a further aspect of the invention there is provided an assay product according to the invention for use with an array reader.

An embodiment of the invention will now be described by example only and with reference to the following figure, materials and methods;

5 Figure 1 is a plasma polymerisation apparatus.

### Materials and Methods

The methodology of plasma polymerisation is disclosed in WO01/31339 and is  
10 incorporated by reference in its entirety.

The schematic diagram of the plasma "writing" equipment is shown in figure 1. Briefly, the reactor comprises two vacuum chambers separated by a Mask Plate, but sharing a common vacuum system. The topmost chamber has several monomer input  
15 ports, and an electrode for exciting a plasma. The lower chamber contains a precision XYZ manipulation stage, upon which is mounted the substrate to be patterned.

The sample is raised so as to be extremely close to the Mask Plate (but without touching). The mask plate consists of a stainless steel plate, with a small aperture  
20 that defines the features to be deposited. The nature of the deposition is such that the plasma is guided by the aperture and forms a polymeric deposit on the surface beneath it. Note however, that this aperture is used almost as a 'pen' to write functionalised polymeric material onto the substrate, as opposed to a simple 'stencil' to form an image on the surface.

25

Both chambers are evacuated using a common vacuum system consisting of a turbomolecular pump backed by a two-stage rotary pump. The base pressure of the whole apparatus is  $\sim 10^{-5}$  mbar.

A plasma is excited in the top chamber, by means of an rf generator (Coaxial Power Systems, UK), and by adjusting the flow rate of the monomer/monomers and the power and pulse regime of the plasma the desired plasma composition is selected.

5 "Writing" of plasma polymers as microdots

Allylamine was obtained from Aldrich (UK) and subjected to several freeze-pump-thaw cycles to remove dissolved gases prior to use. Silicon wafer was used as a substrate and after being cleaned with isopropyl alcohol was attached to the XYZ  
10 stage using double-sided sticky tape. A mask consisting of ~10 micron holes was attached to the Mask Plate and the substrate was raised to within a few microns of the Mask Plate.

A monomer flow rate of ~5sccm was set in the top chamber using fine-control needle  
15 valves. Subsequently, a plasma was excited in the top chamber and sustained for around 30 seconds to provide microdots of allylamine plasma polymer on the area of the substrate immediately beneath the mask plate.

Additional dots of carboxylic acid chemical functionality are written alongside the  
20 amine dots by changing the monomer compound from allylamine to acrylic acid.

"Writing" of Plasma Polymers as Microtracks

The method is identical to that described above for plasma microdots. To deposit  
25 microtracks, the plasma composition is kept the same, and the sample is moved beneath the mask plate, effectively using the plasma to 'write' the tracks and features onto the substrate

30



"Writing" of Plasma Gradients:

A functionality gradient was deposited by using two different monomer compounds. Allylamine and acrylic acid were obtained from Aldrich (UK) and subjected to several freeze-pump-thaw cycles to remove dissolved gases. A mask consisting of a single ~10 micron hole was attached to the mask plate, and a piece of silicon wafer as substrate was raised as close as possible to the mask without touching (as described above). Initially, a plasma was excited using only the acrylic acid monomer feed. The mixture of monomer gases was then varied concomitantly with the linear movement of the sample beneath the mask. Hence the initial deposition was comprised wholly of acrylic acid plasma polymer, while later deposition consisted of a mixture of allylamine and acrylic acid, and the final portion of the deposition consisted wholly of allylamine. Thus over the range of motion of the sample during the experiment, the surface composition changed smoothly from one dominated by carboxylic acid groups, to one in which amine groups dominated.

The above examples explain how different types of feature can be produced upon a substrate material. The substrate is not limited to silicon wafer. Practically any substrate material can be used (for example, polymers, glasses, ceramics and metals), and a pattern deposited upon it. The morphology of the substrate merely affects the maximum resolution of the plasma pattern.

Similarly, the patterns described above are for illustrative purposes only. A polymer may be deposited from virtually any compound (particularly organic compounds), provided it can be induced to form a plasma. Typically this means that the compound must be volatile, although this may be done by heating or by use of a carrier gas. Hence a microdot or array thereof, or a microtrack may be produced which contains any chemical functional group and there is no limit to the number of different chemistries that may be deposited onto a single substrate. This is in contrast to previously disclosed methods of patterning plasma polymers, which are only capable of depositing 'monotone' patterns. The written polymer does not necessarily contain

any functional groups at all — a hydrocarbon starting compound will deposit an essentially functionally blank surface. The provision of functionalised patterns on a non-fouling surface can be achieved by writing on a surface which has first been uniformly plasma polymerised by ethylene oxide. Currently disclosed methods for  
5 patterning of plasma polymers do not allow the production of surfaces containing more than one chemistry. In addition, using this method or writing polymer onto a substrate permits formation on surface of closed loops and circuits — an aspect of surface patterning precluded by use of an overlaid mask.

10 Microgradients are not simply limited to bi-functional gradients, any number of monomers could be used to produce continuously varying surface features. Similarly, gradients of other properties can be envisaged; gradients of wettability (from ultra-hydrophobic through to hydrophilic), gradients of crosslink density, adhesivity and variations of thickness. A gradient can be formed which comprises a chemically  
15 continuous region connecting any two or more polymers with different properties, irrespective of what those properties might be. Consider a polymer as occupying a point in an n-dimensional parameter-space. There will always be a direct path between two such points, which is independent of the dimensionality of the parameter space.

20

The examples described above use a feature scale of around 10 microns to illustrate the techniques. In practice it might be required that surfaces are patterned on a millimetre or centimetre scale as an upper boundary, right down to 1 micron at the bottom end.

25

There are many variations that could be made to the plasma system to control the plasma writing process. Plasma may be excited using DC, radiofrequency (pulsed or continuous wave) or microwave radiation, or it may be excited within, or at the tip of a micrometre scale capillary. There may be carrier gases involved for some less-  
30 volatile monomers. Clearly the processes would benefit from a simple computer system to manage the plasma parameters and position of the XYZ stage for improved

- accuracy and automation of the writing process. Further, although the experiments described the plasma as being in a top chamber, and the sample in a lower chamber, this spatial arrangement is arbitrary – the pattern formation requires only that the sample be isolated from the plasma by the mask plate, irrespective of orientation of the components of the system. Similarly, although in this example the sample is moved around beneath the plasma, the only necessity is for movement of the orifice relative to the sample – this may be achieved by motion of either (or both) of these components.
- It is possible to change the plasma composition in the region of the mask by means of applied electric and magnetic fields. These might be used as 'lenses' to further focus the plasma. They may also be used to increase or decrease the relative contributions of the ionic and radical components of the plasma – in extremis reducing the species arriving at the substrate to a collimated beam of radical species, or low energy beam of ions.

In addition to directly depositing onto the substrate material, pretreatments may be employed to clean the surface, or to etch topographic features into the substrate prior to writing. This allows the construction of 3-dimensional functionalised structures on surfaces (for example a 'trench' with amine functional groups deposited along the bottom) in a single process.

There are a number of areas in which these plasma deposited patterns might be used. Microdots and microarrays may be used as microscopic 'test tubes' for chemical or biochemical interactions, for example in genomics and rapid screening of DNA, proteomics, and immunodiagnostics. The deposited functional groups may be used to immobilise entities such as DNA, RNA, proteins, peptides, polypeptides, ligands, proteoglycans, carbohydrates, nucleotides, oligonucleotides. Alternatively, they may act as reaction sites for subsequent derivatisation by chemical means.

The next level up from microdots and microarrays is to generate micropatterns of single functionalities. Stripes, tracks and more complex shapes may be deposited using different functional groups on the same substrate, allowing functional patterns containing different chemistries to exist on the same substrate and also allowing the formation of loops and circuits. These features might be used in microfluidics for transport of tiny volumes of liquid, as 'microvalves', adsorption of tiny quantities of reagent and to control adhesion properties.

Finally microgradients could be used to separate mixtures of biomolecules on the basis of difference in physical or chemical properties. (for example, mass, charge, size, hydrophobicity). This is analogous to gel electrophoresis, and gel permeation chromatography. Conceivably, gradients to separate out identical mixtures by different properties (charge, size, etc.).

The chemistry of the written features may range from non-functional hydrocarbon surfaces (deposited from alkane, alkene, aromatic type compounds) to any other conceivable chemical group. For example, amines, acids, alcohols, ethers, esters, imines, amides, ketones, aldehydes, anhydrides, halogens, thiols, carbonyls, silicones, fluorocarbons. Additionally, plasma polymers which are electrically conducting may be deposited. The only limitation on the functionality incorporated is that there must exist a starting compound that is capable of being induced to exist in the gas phase (with or without heating) at low pressure (above  $\sim 10^{-5}$  mbar). Different chemistries may also be formed using reactive ( $N_2$ ,  $O_2$ ,  $H_2O$ ), or non-reactive (Ar) gases. These gases may also be used to etch features into the substrate – all as part of the same process.

Patterns that contain a mixture of any number of the above functionalities in any combination or arrangement on the same substrate material.

Surfaces that contain gradients of functionality on a scale of centimetres, down to around 10 microns. A gradient is a region of continuous change between two

different chemistries. A gradient can always be constructed between any two regions of different chemistry, in the same way that a straight line can always be drawn through two points in space.

- 5 The polymer micropatterns, microarrays, microgradients and microtracks may be written onto any substrate material. For example, glasses, ceramics, metals, semiconductors, and polymers including (but not limited to) polycarbonate (PC), polystyrene (PS), polyethyleneterephthalate (PET), polymethylmethacrylate (PMMA), polyvinylchloride (PVC), polytetrafluoroethylene (PTFE).

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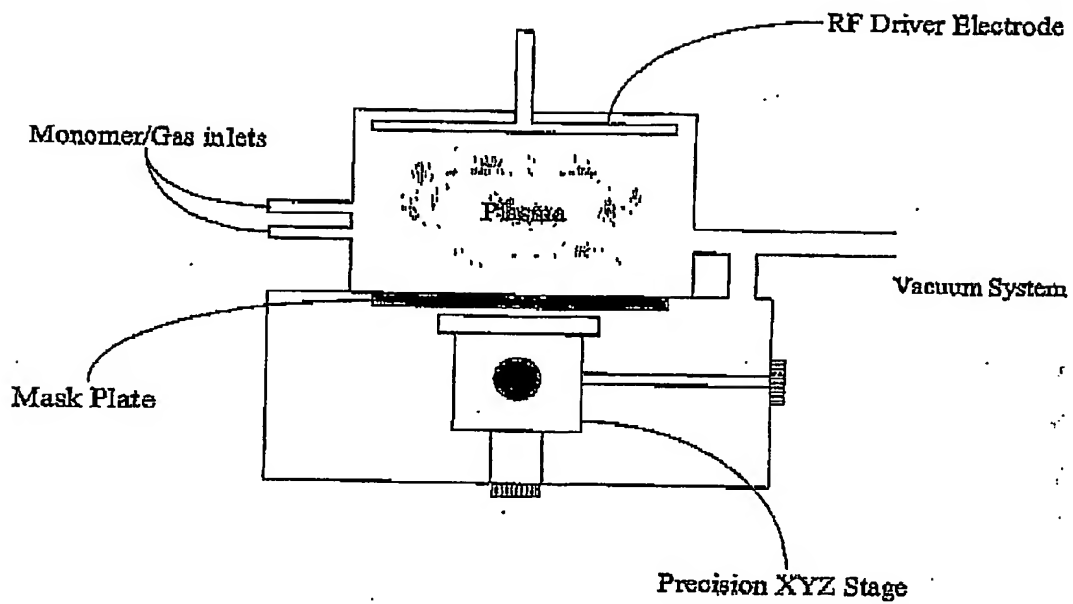
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